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<b>(21) International Application Number:</b> PCT/US96/18984 <b>(22) International Filing Date:</b> 27 November 1996 (27.11.96)  <b>(30) Priority Data:</b> 08/565,943 1 December 1995 (01.12.95) US  <b>(71) Applicants (for all designated States except US):</b> UNIVERSITY OF IOWA RESEARCH FOUNDATION [US/US]; 100 Oakdale Campus #214 TIC, Iowa City, IA 52242-5000 (US). THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 22nd floor, 300 Lakeside Drive, Oakland, CA 94612-3550 (US). AMERICAN CYANAMID COMPANY [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> APICELLA, Michael, A. [-/US]; 2646 Johnsons Crossing, N.E., Solon, IA 52333 (US). SUNSHINE, Melvin, G. [-/US]; 340 Raven Street, Iowa City, IA 52245 (US). LEE, Na-Gyong [-/-]; Apartment 27-1309, Nam-gu Hakik-2-dong, Sindong-a, Incheon (KR). ARUMUGHAM, Rasappa [-/US]; 15 Elatia Circle, Pittsford, NY 14534 (US). GIBSON, Bradford, W. [-/US]; 1324 Peralta Avenue, Berkeley, CA 94702 (US).		<b>(74) Agents:</b> NELSON, M., Bud et al.; Hodgson, Russ, Andrews, Woods & Goodyear, 1800 One M & T Plaza, Buffalo, NY 14203-2391 (US).  <b>(81) Designated States:</b> AU, CA, JP, KR, MX, NZ, US, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> NON-TOXIC MUTANTS OF PATHOGENIC GRAM-NEGATIVE BACTERIA  <b>(57) Abstract</b> <p>A method is provided for identifying, isolating, and producing <i>htrB</i> mutants of gram-negative bacterial pathogens. The method comprises mutating the <i>htrB</i> gene of a gram-negative bacterial pathogen so that there is a lack of a functional <i>htrB</i> protein, resulting in a mutant that lacks one or more secondary acyl chains contained in the wild type gram-negative bacterial pathogen, and displays substantially reduced toxicity as compared to the wild type strain. Also, the present invention provides methods for using a vaccine formulation containing the <i>htrB</i> mutant, the endotoxin isolated therefrom, or the endotoxin isolated therefrom which is then conjugated to a carrier protein, to immunize an individual against infections caused by gram-negative bacterial pathogens by administering a prophylactically effective amount of the vaccine formulation.</p>		